IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of:	Timothy A. Bird, Jacques J. Peschon, John E. Sims, G. Duke Virca and Cynthia R. Willis	Docket No.:	2009-US
		Group Art Unit:	Unknown
		Examiner:	Unknown
Serial No:	--to be assigned--		
Filed:	June 18, 2001		

For: METHODS FOR REGULATING VASCULARIZATION USING GEF CONTAINING NEK-LIKE KINASE (GNK)

BOX PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination of the above-identified application, please amend the application as follows.

In the Specification

Please replace the section at page 1, lines 3-5 with the following section:

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of pending International Application No. PCT/US99/29989, filed 17 December 1999, which was published under PCT Article 21 (2) on 22 June 2000, in English, as WO 00/36097, which claims the benefit of U.S. Provisional Application Serial No. 60/113,003, filed 18 December 1998, now abandoned. International Application No. PCT/US99/29989 and U.S. Provisional Application Serial No. 60/113,003 are incorporated herein by reference.

In the Claims

Please cancel claims 1-52 and add the following new claims (53-77).

53. (New) An isolated nucleic acid encoding a polypeptide comprising a sequence selected from the group consisting of:

(a) SEQ ID NO:2;

(b) sequences at least 80% identical to SEQ ID NO:2, wherein the polypeptide is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4; and

(c) fragments of (a) or (b), wherein the polypeptide is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4.

54. (New) An isolated nucleic acid comprising a sequence selected from the group consisting of:

(a) SEQ ID NO:1;

(b) nucleotides 75-2549 of SEQ ID NO:1;

(c) sequences that are at least 80% identical to (a) or (b), and encode a polypeptide that is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4;

(d) sequences that are capable of hybridizing to (a) or (b) under conditions of moderate stringency, and encode a polypeptide that is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4; and

(e) sequences that are degenerate, as a result of the genetic code, to the sequences of (a), (b), (c), or (d).

55. (New) The nucleic acid of claim 53, selected from the group consisting of:

(a) nucleic acids encoding a polypeptide having the sequence SEQ ID NO:2; and

(b) nucleic acids comprising nucleotides 75-2549 of SEQ ID NO:1.

56. (New) A recombinant expression vector comprising a promoter operably linked to a nucleic acid according to claim 53.

57. (New) A host cell into which the recombinant expression vector of claim 56 has been introduced.

58. (New) A method for producing an sGNK polypeptide comprising culturing the host cell of claim 57 under conditions that promote expression of the polypeptide.

59. (New) An sGNK polypeptide produced according to the method of claim 58.

60. (New) An isolated sGNK polypeptide encoded by a nucleic acid according to claim 54.

61. (New) An isolated sGNK polypeptide comprising a sequence selected from the group consisting of:

(a) SEQ ID NO:2;

(b) sequences at least 80% identical to SEQ ID NO:2, wherein the polypeptide is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4; and

(c) fragments of (a) or (b), wherein the polypeptide is capable of binding to and/or being phosphorylated by a GNK polypeptide having the sequence SEQ ID NO:4.

62. (New) The polypeptide of claim 61 comprising the sequence of SEQ ID NO:2.

63. (New) A sGNK polypeptide selected from the group consisting of:

(a) oligomers comprising at least one polypeptide according to claim 61; and

(b) conjugates comprising at least one polypeptide according to claim 61.

64. (New) A method of identifying a compound that modulates a protein-protein interaction between the sGNK polypeptide of claim 61 and a GNK polypeptide, comprising:

(a) contacting a candidate compound with the sGNK and GNK polypeptides under conditions permitting the interaction of the polypeptides; and

(b) measuring the ability of the candidate compound to modulate the protein-protein interaction.

65. (New) A method of identifying a compound that modulates phosphorylation of the sGNK polypeptide of claim 61 by a GNK polypeptide, comprising:

(a) contacting a candidate compound with the sGNK and GNK polypeptides under conditions permitting phosphorylation of sGNK by GNK; and

(b) measuring the ability of the candidate compound to modulate the phosphorylation of sGNK by GNK.

66. (New) A method of identifying a compound that modulates vascularization comprising:

(a) contacting a candidate compound with the sGNK polypeptide of claim 61 and a GNK polypeptide; and

(b) measuring the ability of the candidate compound to modulate a biological activity of the sGNK and/or GNK polypeptides.

67. (New) A homologous recombination vector comprising a nucleotide sequence substantially similar to SEQ ID NO:3, the sequence differing from SEQ ID NO:3 by the addition, deletion, or substitution of one or more nucleotides to prevent expression of a polypeptide with vascularization regulatory capability, structurally linked to one or more selectable marker genes.

68. (New) The homologous recombination vector of claim 67 wherein at least one selectable marker gene confers resistance to G418.

69. (New) The homologous recombination vector of claim 67 wherein at least one selectable marker gene confers sensitivity to ganciclovir.

70. (New) A method of generating GNK-deficient cells comprising:

(a) introducing the homologous recombination vector of claim 67 into a cell;

(b) selecting for cells into which the homologous recombination vector has been introduced;

(c) propagating the selected cells; and

(d) monitoring the propagated cells for GNK expression.

71. (New) A nonhuman transgenic embryo, fetus, or animal that is heterozygous for a targeted mutation in a GNK polypeptide having the sequence SEQ ID NO:4.

72. (New) A nonhuman GNK-deficient embryo, fetus, or animal produced by crossing heterozygous animals of claim 71.

73. (New) A cell from the embryo, fetus, or animal of claim 71.

74. (New) A cell from the embryo, fetus, or animal of claim 72.

75. (New) An antibody or fragment thereof which binds specifically to a polypeptide according to claim 61.

76. (New) The antibody or fragment of claim 75 wherein the antibody is a polyclonal antibody.

77. (New) The antibody or fragment of claim 75 wherein the antibody is a monoclonal antibody.

REMARKS

Applicants have amended the first section of the specification to update the cross-reference to related applications. A marked up version of the replacement section is shown in the Appendix entitled "VERSION WITH MARKINGS TO SHOW CHANGES."

Applicants have cancelled claims 1-52 and added claims 53-77. No new matter has been added.

Claims 1-5, 51, and 52 have been rewritten as claims 53-57. Claims 53-57 are supported by claims 1-5, 51, and 52 and throughout the specification, in particular, at page 13, line 6 to page 17, line 10, at page 9, lines 5-29, at page 36, lines 5-7, and at page 10, line 20 to page 12, line 16. Claim 58 is newly added, and is supported throughout the

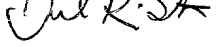
specification and, in particular, at page 12, line 17 to page 13, line 5, and at page 21, line 14 to page 27, line 6.

Claims 6-9 have been rewritten as claims 59-63. Claims 59-63 are supported by claims 6-9 and throughout the specification, in particular, at page 12, line 17 to page 13, line 5, at page 21, line 14 to page 27, line 6, and at page 15, line 11 to page 21, line 13.

Claims 31-33, 35-38, 41-44, and 46-48 have been rewritten as claims 64-77. Claims 64-77 are supported by claims 31-33, 35-38, 41-44, and 46-48 and throughout the specification.

Applicants respectfully submit that pending claims 53-77 are in condition for allowance. If a telephone interview would be helpful in advancing the prosecution of this application, Applicants' attorney invites the Examiner to contact her at the number provided below.

Respectfully submitted,



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APPENDIX
VERSION WITH MARKINGS TO SHOW CHANGES

In the Specification

The following is a marked up version of the section at page 1, lines 3-5.

~~**CROSS-REFERENCE TO RELATED APPLICATION**~~

~~The present application claims the benefit of U.S. Provisional Application No. 60/113,003, filed December 18, 1998, which is hereby incorporated by reference.~~

CROSS REFERENCE TO RELATED APPLICATIONS

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